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W/Cook 4/15/05

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## REMARKS

The invention as presently claimed relates to assay devices for determining the presence or amount of an analyte of interest in a sample, and kits containing such devices. The devices of the present invention comprise, *inter alia*, the following elements: (i) a reaction chamber comprising an optically detectable label; (ii) a diagnostic lane comprising at least one assay zone configured to bind the analyte of interest, and at least one timing zone; (iii) an optical component configured to detect an optical signal generated from the timing zone and generate an electronic signal in response; and (iv) a signal processor configured to read the electronic signal and determine the progress of the assay and its time of completion.

\* A signal obtained from the timing zone of the present invention "allows the instrument to judge when the assay process is complete." Specification, page 40, lines 18-19. The "timing zone" referred to in the instant claims is described in the specification as one embodiment of "independent assay controls" (IAC) for use in monitoring and performing assays. IACs provide a measurable signal that is generated in connection with, but that is independent of, the signal obtained from the assay for an analyte of interest.

Claims 27, 28, and 93-128 are pending. The Examiner has indicated that claims 97, 98, 105, 106, 119, and 120 would be allowable if written in independent form. Claims 27, 93, 101, 113, and 115 have been amended herein. The specification provides support for an assay zone separate from a timing zone (e.g. page 15, lines 19-28). The amendments raise no issue of new matter. It is noted that the amendments of the claims have not been made to obviate prior art but rather have been made to emphasize features of the invention for better understanding by the examiner.

Notwithstanding the foregoing, Applicants expressly reserve the right to prosecute matter no longer or not yet presented in one or more applications that may claim priority hereto. Applicants respectfully request reconsideration of the claimed invention in view of the following remarks.

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Non Art-Related RemarksObjection to the Drawings

The drawings are objected to under 37 C.F.R. § 1.83 (a) because they allegedly do not show every feature of the invention specified in the claims. A proposed drawing correction or corrected drawings have been required of Applicant to avoid abandonment of the application.

It is respectfully submitted that the objection is unfounded. First, the Examiner has not identified any specific feature of the current figures that is lacking. Applicant cannot respond to the objection unless a specific basis is provided. Second, all the features of the presently claimed apparatus and kit (e.g., reaction chamber, diagnostic lane, assay zone) are thoroughly described and need not be exemplified in a drawing. Drawings are only required "where necessary" for the understanding of the subject matter sought to be patented. 37 C.F.R. § 1.81 (a) (emphasis added).

Nevertheless, in an effort to advance prosecution, Applicants submit in a separate paper (filed concurrently with the instant amendment) a drawing showing the features specified in the claims.

OK!  
L. Lock35 U.S.C. § 112, Second Paragraph (Rejection Maintained)

Applicants respectfully traverse the rejection of claims 27, 28, and 93-128 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite "because the use of the 'timing zone' is vague and indefinite because it is not clear as to what this term is to encompass." Paper No. 24, page 4. It is further alleged that a "timing zone" is a "relative term," not defined by the claim, and not supported in the specification with a standard for determining the requisite degree.

When determining definiteness, the proper standard to be applied is "whether one skilled in the art would understand the bounds of the claim when read in the light of the specification." *Credle v. Bond*, 30 USPQ2d 1911, 1919 (Fed. Cir. 1994). Recognizing that the English language

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is not always precise, the settled law has established that the essential inquiry in a definiteness analysis is whether the claims set out and circumscribe the claimed subject matter with reasonable particularity. See, e.g., MPEP § 2173.02; see also, *Miles Laboratories, Inc. v. Shandon, Inc.*, 27 USPQ2d 1123, 1127 (Fed. Clr. 1993) ("If the claims read in the light of the specification reasonably apprise those skilled in the art of the scope of the invention, § 112 demands no more.") (emphasis added). Definiteness is not analyzed in a vacuum, but in light of the content of the specification, and with the knowledge available to the skilled artisan.

As discussed above, the present claims refer to devices for measuring the presence or amount of at least one analyte. The "timing zone" referred to in the instant claims is described in the specification as one embodiment of "independent assay controls" (IAC) that provide a measurable signal that is generated in connection with, but that is independent of, the signal obtained from the assay for the analyte of interest. As described in the instant specification, e.g., beginning on page 73, section entitled "Use of the Timing Signal to Detect Assay Completion of Immunoassay Devices," the phrase "timing zone" refers to an element of the claimed assay devices where a signal is detected for use in determining if the assay for the analyte of interest has run to completion. Methods and devices for determining the progress and time of completion of such an assay using a signal obtained from a "timing zone" are described in detail in the instant specification, e.g., on page 13, line 7, through page 14, line 15; page 40, line 9, through page 42, line 23; and page 73, line 6, through page 75, line 30.

First, the device configuration described in the claims clearly comports with the meaning of the "timing zone" as described in the specification. For example, part (a) of claim 27 recites a diagnostic lane comprising a timing zone; part (b) indicates that an optical component is configured to detect an optical signal from a label at the timing zone and to generate an electronic signal in response; and part (c) indicates that a signal processor is configured to determine the progress and time of completion of an analyte assay from the electronic signal.

Considering the extensive teachings in the instant specification concerning the design and use of timing zones to determine if an assay has run to completion, and the literal language of the claims, Applicants respectfully submit that the skilled artisan is reasonably apprised of the scope

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of the claims with regard to the phrase "timing zone" as used in the instant claims. As noted above, it is well settled that 35 U.S.C. § 112, second paragraph, demands no more.

In contrast, the Examiner continues to assert, without support or explanation, that the phrase "timing zone" should be considered a "relative term." See Paper No. 19, page 3, last paragraph, and paper 24, page 4. The Examiner has been requested and has failed to provide any objective evidence or reasoning for why the skilled artisan would consider a "timing zone" to be a relative term. It is respectfully submitted that there is nothing relative about a zone that provides a signal used to determine the progress and time of completion of an analyte assay. Moreover, the Examiner's assertion that, because "the term 'timing zone' is not defined by the claim" (*id.*), the claim is rendered indefinite, is at odds with the requirement that the claims be interpreted in the light of the specification and viewing the claim as a whole. See, e.g., MPEP § 2173.02. In the instant case, the phrase "timing zone" should not be interpreted in a vacuum, but must be interpreted in light of the extensive teachings in the instant specification, the clear interrelation of the optical component and the signal processor with the timing zone in the claims, and from the point of view of one possessing the ordinary level of skill in the art. When properly considered in this light, the instant claims meet the definiteness standard of 35 U.S.C. § 112, second paragraph.

In view of the foregoing, Applicants respectfully submit that the skilled artisan is reasonably apprised of the scope of the claims with regard to the phrase "timing zone" as used in the instant claims. Thus, because the definiteness requirement of 35 U.S.C. § 112, second paragraph, has been met, Applicants respectfully request that the rejection be reconsidered and withdrawn. If not withdrawn, the Examiner is respectfully urged to specifically address Applicants' arguments and provide support for the asserted allegations.

35 U.S.C. § 112, Second Paragraph (New Grounds of Rejection)

A. Applicants respectfully traverse the rejection of claims 27, 28, and 93-128 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite "because the interaction of the timing zone is unclear." Paper No. 24, page 5. The standard for definiteness is discussed directly above.

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Contrary to the Examiner's assertion that "the relations between [the assay zone and the timing zone] is not recited" and that "it is not clear that the timing zone is located down stream from the assay zone" (Paper No. 24, page 5), Applicants respectfully submit that no particular relationship between the two zones is described by the specification as being required, and that the breadth of the claim in this regard is not indefinite. For example, the skilled artisan would understand that the timing zone may be placed at the distal end of the diagnostic lane (described as a preferred embodiment of the invention; *see, e.g.*, specification, page 41, lines 11-15). But the timing zone might also be placed parallel to the assay zone, or may even precede the assay zone. If made necessary by positioning of the timing zone in the device, the criteria for a measurement at the timing zone that defines assay completion may be derived empirically. *See, e.g.*, specification, page 41, lines 22-23.

Likewise, Applicants respectfully submit that the Examiner's assertion that "the label does not clearly bind to either of the zones to produce a detectable product" (Paper No. 24, page 5) is not relevant to the definiteness of the claims, and fails to consider the extensive teachings of the specification on the subject. The claims clearly state that the diagnostic lane comprises "at least one assay zone configured to bind said analyte." The claims do not require that the label generating a signal at the timing zone bear any relation to any signal obtained at the assay zone. Numerous methods are known in the art for detection of analytes in such assays, and examples of such methods are described in the specification. With regard to the timing zone signal itself, the specification clearly informs the artisan that no binding of the label to the timing zone is required. While binding of the label to the timing zone is one embodiment of the present invention, all that is required by the claims and the specification is that one measure a signal in the timing zone. For example, that signal may be generated from label flowing through the timing zone. *See, e.g.*, specification, page 71, lines 4-6.

The claims clearly state that the device comprises (i) a timing zone; (ii) an optical component configured to detect an optical signal generated from a label in the timing zone and generating an electronic signal in response; and (iii) a signal processor configured to receive the electronic signal and to determine said progress and time of completion of said assay. Applicants

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have amended the claims herein to explicitly state that, when fluid comprising a detectable label is added to the device, the detectable label flows with the fluid to contact the timing zone.

Applicants submit that this amendment is made for the benefit of the Examiner's understanding of the claims, and that this amendment does not alter the scope of the claims. \*

Considering the extensive teachings in the instant specification concerning the design and use of timing zones to determine if an assay has run to completion, and the literal language of the claims, Applicants respectfully submit that the skilled artisan is reasonably apprised of the scope of the claims in this regard. As noted above, it is well settled that 35 U.S.C. § 112, second paragraph, demands no more. Thus, because the definiteness requirement of 35 U.S.C. § 112, second paragraph, has been met, Applicants respectfully request that the rejection be reconsidered and withdrawn.

B. Applicants also respectfully traverse the rejection of claims 93, 101, and 115 for reciting the phrase "electrical and/or magnetic signal." The phrase "and/or" in a claim is broad, not indefinite. See, e.g., *Ex Parte Nilssen*, Appeal No. 96-3618, page 10 (Bd. Pat. App. Int. 1996) (for the convenience of the Examiner, Applicants note that this decision is available at <http://www.uspto.gov/web/offices/dcom/bpai/decisions/fd963618.pdf>). Moreover, contrary to the Examiner's opinion that "it is not clear as to how the signal can be electrical and magnetic at the same time" (Paper No. 24, page 5), the electrical and magnetic properties of a given label are simply two physical parameters, each of which could be measured separately or together. The Examiner is requested to provide objective evidence supporting the assertion that such properties must be measured exclusively of one another should the rejection be maintained.

In an effort to advance prosecution, however, the phrase "electrical and/or magnetic signal" has been replaced by amendment with the separate phrases "electrical signal," "magnetic signal," and "electrical and magnetic signals." Because the definiteness requirement of 35 U.S.C. § 112, second paragraph, has been met with regard to this language, Applicants respectfully request that the rejection be reconsidered and withdrawn.

35 U.S.C. § 112, First Paragraph

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Applicants respectfully traverse the rejection of claims 27, 28 and 93-128 under 35 U.S.C. § 112, first paragraph, as allegedly failing to satisfy the written description requirement with regard to the phrase "at least one timing zone separate from the assay zone." The Examiner invites Applicants to point out where the specification supports this phrase.

The proper standard for determining compliance with the written description requirement of 35 U.S.C. § 112, first paragraph, is whether the specification reasonably conveys to the skilled artisan that the inventor was in possession of the claimed invention as of the filing date. See MPEP § 2163.02 (citing *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 227 USPQ 177, 179 (Fed. Cir. 1985)). The subject matter of the claimed invention need not be described literally in the specification in order to satisfy the requirements of 35 U.S.C. § 112, first paragraph. *Id.* In a careful analysis of the written description requirement provided by Patent and Trademark Office in its *Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112 ¶1, "Written Description" Requirement*, it is stated that an adequate written description "may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention." 66 Fed. Reg. 1099, 1105 (2001) (emphasis added).

In describing the claimed invention, the specification states that the progress and time of completion of an assay, a timing zone signal is measured at "a discrete zone" in the diagnostic lane. See, e.g., specification, page 13, lines 11-15; page 41, lines 6-10; and page 42, lines 2-4. The specification also states that the assay measurement may be made in one zone, and the IAC signal (e.g., the timing zone signal) can be measured in another zone. See, e.g., specification, page 13, lines 19-21. The specification also provides an example where the timing zone is "downstream of the last detection zone"; thus, in this example, the timing zone is separate from the assay zone. See, e.g., specification, page 71, lines 2-4.

Thus, Applicant respectfully submits that reference to the above cited portions of the specification readily demonstrates support for the limitation "at least one timing zone separate from the assay zone." Because the written description requirement of 35 U.S.C. § 112, first paragraph, has been met, Applicants respectfully request that the rejection be reconsidered and

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withdrawn.

Art-Related Remarks35 U.S.C. §103

I. Applicants respectfully traverse the rejection of claims 27, 93, 94, 96, 99-100, 109-116, 118, and 121-126 as allegedly being unpatentable over Buechler *et al.*, U.S. Patent No. 5,458,852 ("the '852 patent") in view of Van Deusen *et al.*, U.S. Patent No. 5,132,097 ("the '097 patent"). Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness.

To establish a *prima facie* case of obviousness, three criteria must be met; there must be some motivation or suggestion, either in the cited publications or in knowledge available to one skilled in the art, to modify or combine the cited publications; there must be a reasonable expectation of success in combining the publications to achieve the claimed invention; and the publications must teach or suggest all of the claim limitations. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991); MPEP § 2142. In analyzing obviousness, the Court of Appeals for the Federal Circuit has repeatedly cautioned that:

[t]he factual inquiry... must be based upon objective evidence of record.... [T]he best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references.... [P]articular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed.

*In re Sang-Su Lee*, 277 F.3d 1338, 1343 (Fed. Cir. 2002) (internal citations omitted).

As described above, the devices of the present invention comprise, *inter alia*, the following elements: (i) a reaction chamber comprising an optically detectable label; (ii) a diagnostic lane comprising at least one assay zone configured to bind the analyte of interest, and at least one timing zone; (iii) an optical component configured to detect an optical signal generated from the timing zone and generate an electronic signal in response; and (iv) a signal



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processor configured to read the electronic signal and determine the progress of the assay and its time of completion. See, e.g., claim 27.

The Examiner begins the obviousness analysis with a flawed perspective of the cited art, stating that the primary '852 patent discloses "a time gate for measuring the reaction in a given period of time." Paper No. 24, page 7, emphasis added. As Applicants discussed in detail previously, however, this interpretation of the time gate disclosed in the '852 patent is not supported by the '852 patent. For example, column 7, lines 41-45 of the '852 patent defines a time gate as follows:

#### Time Gate

Referring to FIG. 1a, the time gate 5 holds the reaction mixture in the reaction chamber 4 for a given period of time. The concept of the time gate is that a predominantly aqueous solution cannot pass through a hydrophobic zone until the hydrophobic zone is made hydrophilic.

As is made clear by this definition, the "time gate" of the '852 patent is not involved in *measuring* any reaction, contrary to the Examiner's position.

The obviousness analysis is further founded on the faulty understanding that the instant claims can be reduced to a few simple elements: a zone in a diagnostic lane separate from an assay zone, an optical detector, and a signal processor. Applicants respectfully submit that this is an incorrect interpretation of the instant claims. For example, the Examiner states that "the timing zone merely has to be apart [sic: believed to be 'a part'] of the diagnostic lane and separate from the assay zone." Paper No. 24, page 11. While a true statement, it does not provide a complete analysis of the meaning of the phrase "timing zone." As discussed in detail in Applicants' previous response, a "timing zone" is a zone in the claimed device from which a signal indicating the progress of an assay and its time of completion is obtained by the optical component of the claim. The Examiner's simplified view of the claimed invention is improperly founded, as the ordinary skilled artisan would consider the claimed "timing zone" to be much more than a "zone" on a diagnostic lane separate from the assay zone.

In contrast to the "timing zone" of the instant claims, the "time gate" disclosed in the

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'852 patent is not configured to provide any signal whatsoever, much less a signal indicating the progress of the assay and its time of completion (as required in order to meet the limitation of a "timing zone"). While the Examiner takes the position that this fact is allegedly irrelevant "because the instant disclosure teaches the same inventive concept with respect to the claimed apparatus" (Paper No. 24, page 11), Applicants respectfully submit that what the *instant disclosure* teaches is not relevant to the obviousness analysis. The *prima facie* case must be based on the prior art, and without reference to the instant specification. Moreover, Applicants respectfully request that the Examiner provide a reference to *any* statement in the '852 patent disclosing that a "time gate" is "a part of the diagnostic lane" as the Examiner apparently believes.

Likewise, the Examiner appears to believe that that the language in the claims referring to an optical component *configured to detect* an optical signal generated from a label in the timing zone and generate an electronic signal in response, and a signal processor *configured to receive* the electronic signal and to determine the progress and time of completion of an assay, represent "recitation with respect to the manner in which a claimed apparatus is to be employed" (Paper No. 24, page 12), which can be ignored to reduce the claim elements to simply an optical component and a signal processor. Applicants respectfully submit that this language in the claims cannot be ignored, and that the configuration of the optical component and the signal processor within the claimed devices represent structural elements that must be considered by the Examiner.

The failure to properly consider the claims in this regard represents a fundamental flaw in the Examiner's asserted *prima facie* case. The instant claims require a timing zone, an optical component configured to detect an optical signal generated from a label in the timing zone and generate an electronic signal in response, and a signal processor configured to receive the electronic signal and to determine the progress and time of completion of an assay. In order to establish a *prima facie* case of obviousness, such elements must either be present in the publications cited by the Examiner (together with a motivation to combine the publications), or a motivation must be provided to modify the cited publications to provide such elements. That

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motivation must come from the prior art, and not from a reference to the instant disclosure.

Because the primary '852 patent does not contemplate generating any signal from the disclosed "time gate," these claim elements are neither disclosed nor suggested in the '852 patent. The Examiner relies on the secondary '097 patent solely for the alleged disclosure of "an optical signal detector and signal processor." Paper No. 24, page 12. Simply combining these publications to place an optical signal detector and signal processor in a device with a "time gate" as defined in the '852 patent is not sufficient to meet all of the limitations of the instant claims. Rather, the optical signal detector and signal processor must be configured with a timing zone in the manner claimed. Because neither publication of record discloses or suggests that any signal should be obtained from a discrete timing zone or that a signal processor should be used to determine the progress and time of completion of an assay from that signal, the fundamental elements of an obviousness rejection -- a teaching or suggestion of each element of the claims and a motivation to modify the cited publications to provide the invention as claimed -- are lacking from the Examiner's asserted *prima facie* case.

The Examiner's rejection is further flawed by a continued reliance on additional mischaracterizations of the art of record and of the standard by which modifications to the art of record may be considered obvious. For example, referring to the devices disclosed in the '852 patent, the Examiner states that "the rate of change is monitored by the flow of reagents through the porous member." Paper no. 26, page 7. As discussed previously, the text cited by the Examiner in support of this statement (column 18, lines 2-8 of the '852 patent) is devoid of support for the Examiner's statement. Then, referring to possible modifications of devices disclosed in the '852 patent, the Examiner states that "the label (signal development element) does not appreciably bind to any reagent in the assay device but could be designed to indirectly cause a visually or instrumentally detectable signal as a result of the assay process" Paper No. 26, page 7, emphasis added. Applicants respectfully submit that the mere fact that the devices of the primary '852 patent *could be designed* to meet some limitation of the present claims does not establish that such devices meet the requirements of the instant claims, or provide a motivation to modify the devices of the cited publication. To establish a motivation to modify the prior art, the

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Examiner must provide some motivation or suggestion, either in the cited references or in knowledge available to the ordinarily skilled artisan to do so (*see, e.g.*, MPEP §2143), rather than simply stating that such a modification *could be made*.

Finally, the Examiner states that "one cannot show nonobviousness by attacking references individually where rejections are based on combinations of references." Paper No. 24, page 12. Applicants respectfully submit that the Examiner's recitation of this well established principle of patent law does not alter the flaws in the asserted *prima facie* case discussed above. The devices of the instant claims comprise a timing zone, an optical component configured to detect an optical signal generated from a label in the timing zone and generate an electronic signal in response, and a signal processor configured to receive the electronic signal and to determine the progress and time of completion of an assay. Nothing in the cited patents, whether considered separately or in combination, discloses or suggests such devices.

Because the cited patents, taken individually or in combination, fail to teach or suggest each and every element of the instantly claimed invention, Applicants respectfully request that the rejection under 35 U.S.C. § 103 be reconsidered and withdrawn.

II-IV. Applicants also respectfully traverse the rejection of claim 95 and 117 as allegedly being unpatentable over the primary '852 patent in view of the secondary '097 patent and in further view of Slovacek *et al.*, U.S. Patent No. 5,242,837 ("the '837 patent"); of claims 28, 101, 102, and 104, 107, 108, 127, and 128 as allegedly being unpatentable over the primary '852 patent in view of the secondary '097 patent and in further view of Foster *et al.*, U.S. Patent No. 4,444,879 ("the '879 patent"); and of claim 103 as allegedly being unpatentable over the primary '852 patent in view of the secondary '097 patent and in further view of both the '837 and '879 patents.

The Examiner's flawed *prima facie* case of obviousness regarding the primary '852 and secondary '097 patents also underpins the obviousness rejections of these claims. As in the rejections now withdrawn in view of Applicants' Appeal Brief, the Examiner merely contends that the further secondary '837 and '879 patents disclose the use of fluorometers and the provision of assay reagents as kits, respectively. Paper No. 19, pages 7-9.

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Thus, for the same reasons discussed in detail above, the Examiner has failed to meet the burden of establishing a *prima facie* case of obviousness. Because the cited patents, taken individually or in combination, fail to teach or suggest each and every element of the instantly claimed invention, Applicants respectfully request that the rejection of these claims under 35 U.S.C. § 103 be reconsidered and withdrawn.

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**CONCLUSION**

In view of the foregoing remarks, Applicants respectfully submit that the pending claims are in condition for allowance. An early notice to that effect is earnestly solicited. Should any matters remain outstanding, the Examiner is encouraged to contact the undersigned at the telephone number listed below so that they may be resolved without the need for additional action and response thereto.

Respectfully submitted,

Date August 18, 2004By Barry Wilson

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